A proposed modification to the structure of DNA: Testing Mark Curtis's Hypothesis

Mark Curtis

UK

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Introduction

DNA takes the Shape of a twisted ladder. The DNA molecule consists of two nucleotide chains that swirl around one another to form a double helix carrying the genetic information. Each nucleotide is composed of one of the four nucleobases (Adenine, Thymine, Cytosine or guanine.) a sugar called deoxyribose and a phosphate group. The nucleotides are linked to one another in a chain by covalent bonds between the sugar of one nucleotide and phosphate group of the other, resulting in an alternating sugar-phosphate backbone. The nucleobases of the two polynucleotide strands are connected to each other following base pairing rules (A with T and C with G), with hydrogen bonds to make double standard DNA, that holds the double helix in shape. A British artist named Mark Curtis discovered a hypothesis by working on his own series of drawings and paintings of DNA. Curtis never proved anyone wrong. But the result of his artistic imagination is truly radical. Curtis has discovered a new model that he claims it works far better than Watson and Crick's model. Curtis model began with a decagon-a 10-sided figure. He then kept a pentagon for each of the base around it (as shown in the diagram). He observed that the Pentagon is the only regular shape to fit around a decagon in this way without having any space. And Curtis proposed that this figure of 10 pentagons oriented about a decagon is the only geometrical configuration that enables to create a helix that matches the known dimensions of DNA. Curtis established that a double helix of 10 turns had to be made of twinned pentagons. In the standard Watson and Crick model, the base pairing is through hexagonal regions in their structures but in Curtis's theory, the molecular structures of the bases also have pentagons in them. Curtis discovered the model with two pentagons, building a consistent helix that conformed to the dimensions of the DNA double helix." By connecting the nucleobases in a different way, Curtis noticed that he has naturally formed pairs of pentagons in each base

pair. Once the bases were rearranged in their new configuration, the new model simply comes out of its own accord. Watson and Crick established that DNA is a double helix, but Curtis in his hypothesis established why it should take that geometry. In this article, it is predicted that Curtis model derives greater stabilization energy from base stacking than does the Watson - Crick Model in the presence of water.

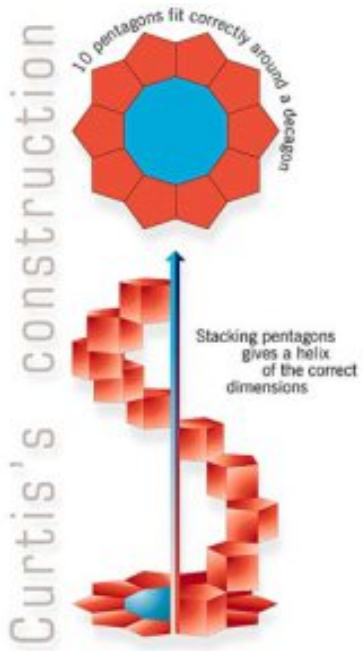

Curtis's construction
10 pentagons fit correctly around a decagon
Stacking pentagons gives a helix of the correct dimensions

Figure 1. The ten pentagons taking round to fit on a hexagon and forming a natural helix

Hypothesis

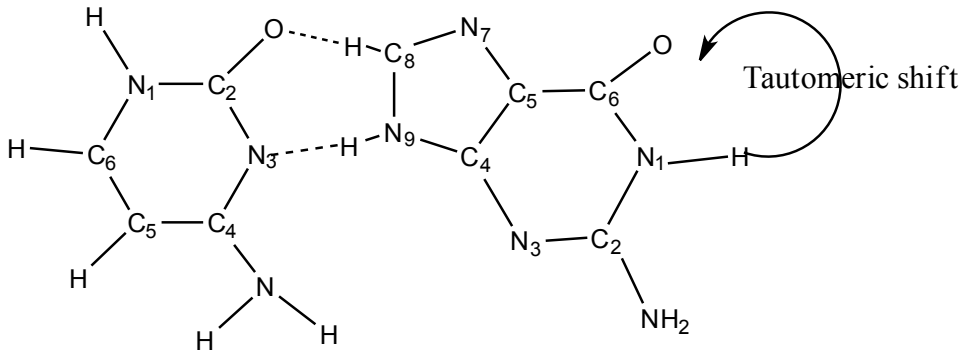
To test the modified structure of DNA proposed by Mark Curtis.

Materials and Method

The alternative base pairing has been tested by simulating Adenine, Thymine, Guanine, and Cytosine in **ChemBio3D software** using **MM2 force field algorithm** developed by Norman Allinger [1, 2, 3, 4]. For free interaction of molecules in space in vacuum, **Consistent Force Field (CFF) algorithm** was used. CFF algorithm is a family of force fields adapted to a broad variety of organic compounds, including force fields for

polymers, metals, etc. [6,7,8]. The **Ascalaph Designer package software with AMBER94 force field algorithm** was used to simulate the molecular interaction dynamics in the aqueous environment [9,10]. All the diagrams were prepared using the Chem3D and ChemDraw programs (Cambridge Soft Corporation).

Then the experiment begins with the base pairs belonging to Mark E. Curtis, Shown in figure 2 and figure 3. Next experiment is done for simulation of Adenine and Thymine base pairing proposed by Mark E. Curtis (Figure 4). Likewise, simulation has been done for Watson Crick base pairings (AT and GC) (Figure 5).



CURTIS BASE PAIRING

Figure 2

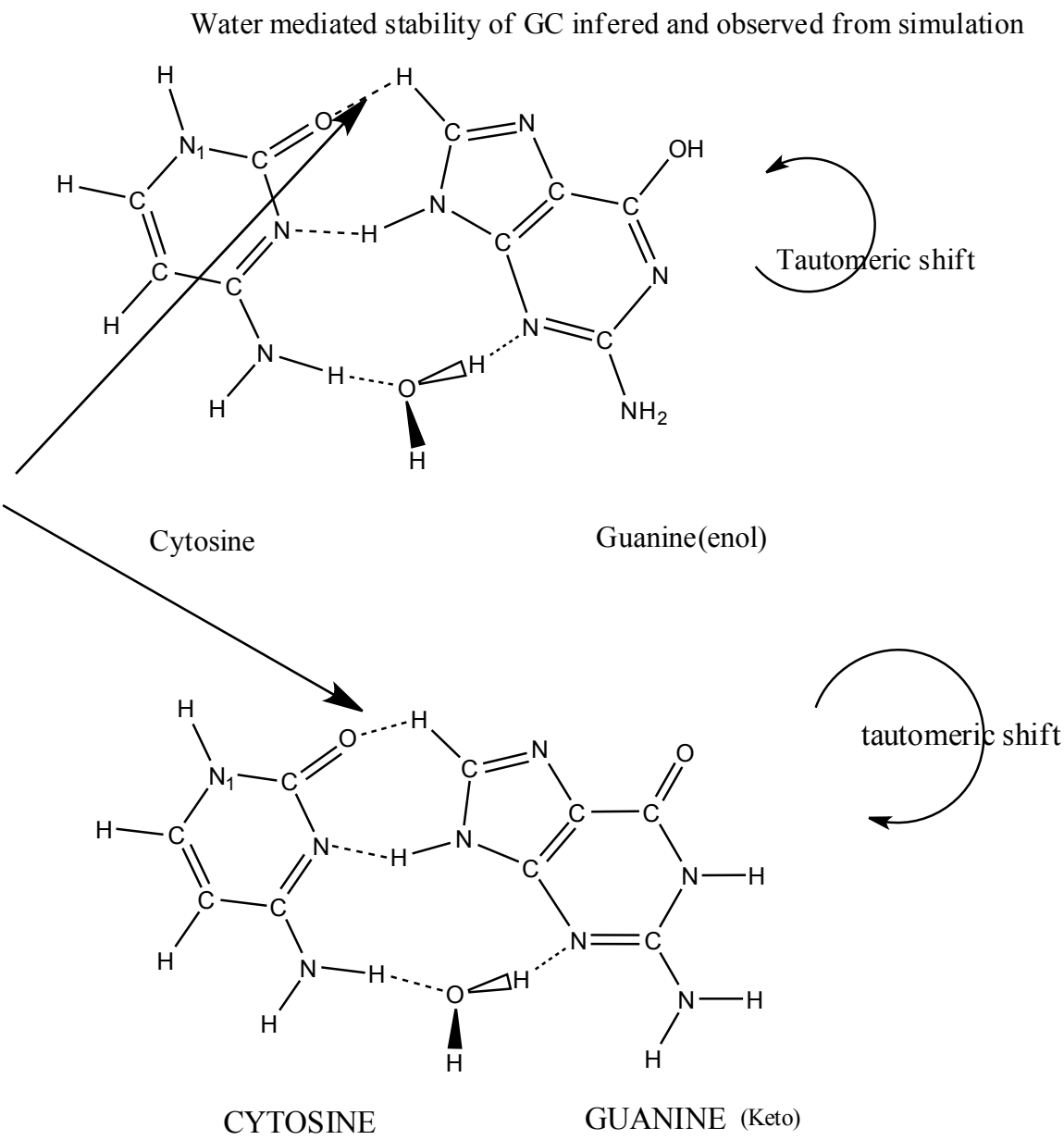
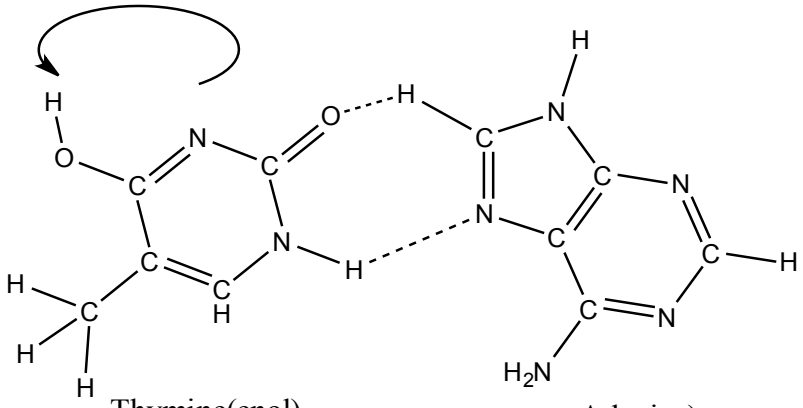
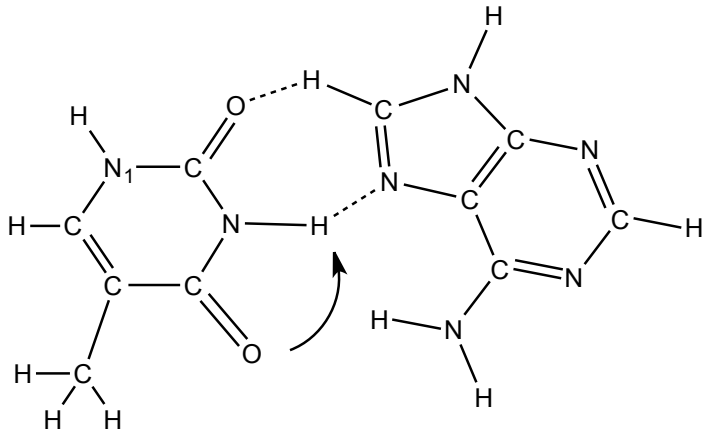

Water mediated stability of GC infered and observed from simulation
Tautomeric shift
Cytosine
Guanine(enol)
tautomeric shift
CYTOSINE
GUANINE (Keto)

Figure 3



Thymine(enol) Adenine)

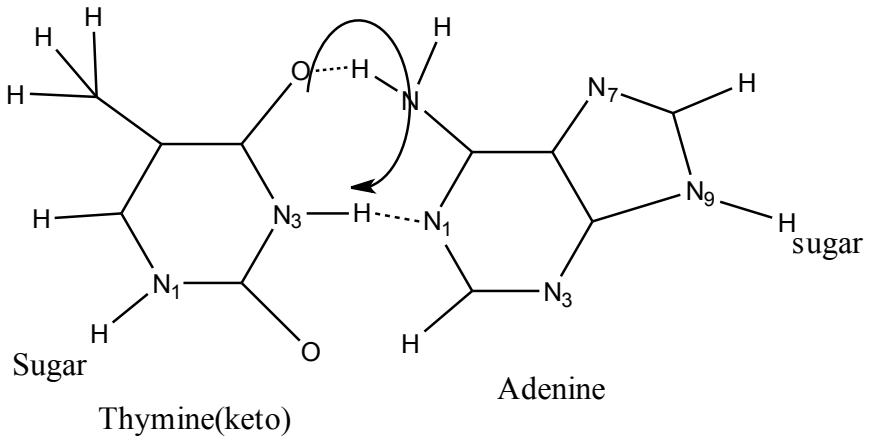


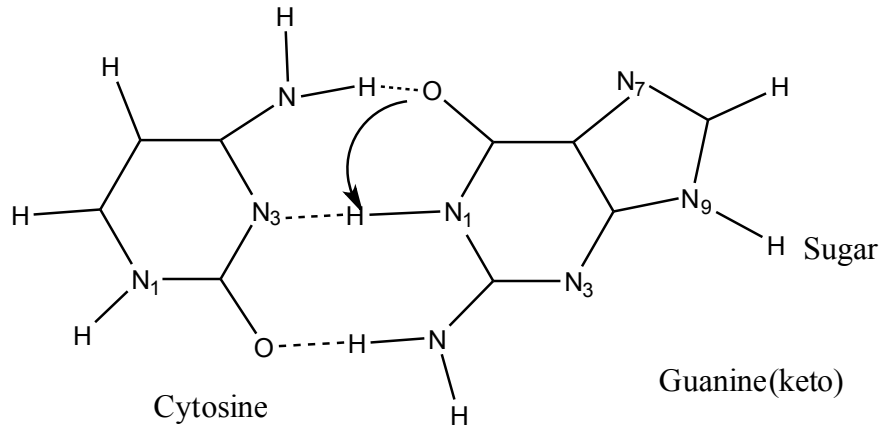
(Adenine)

Thymine keto

Curtis proposed Basepairing of Adenine Thymine

Figure 4

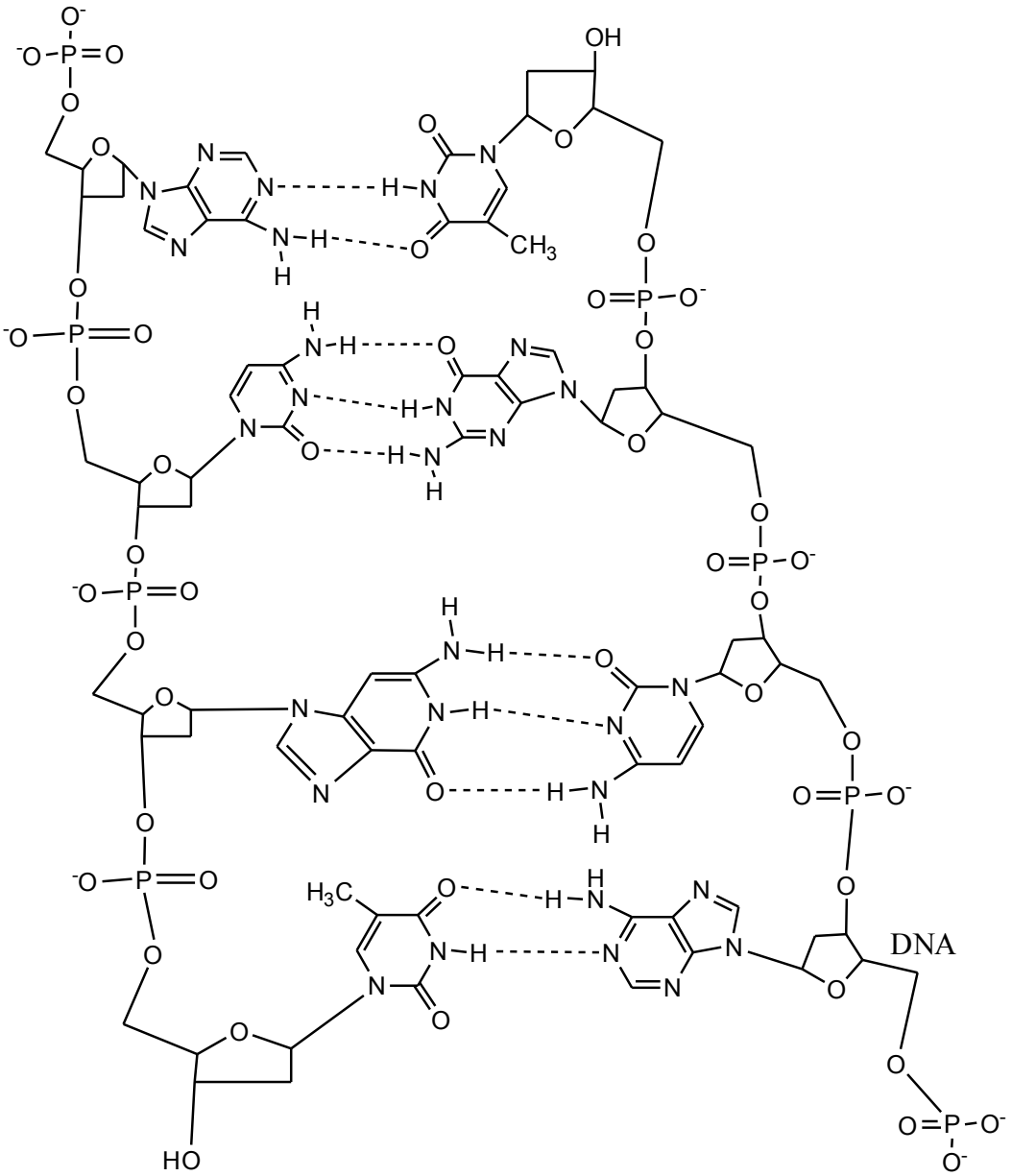


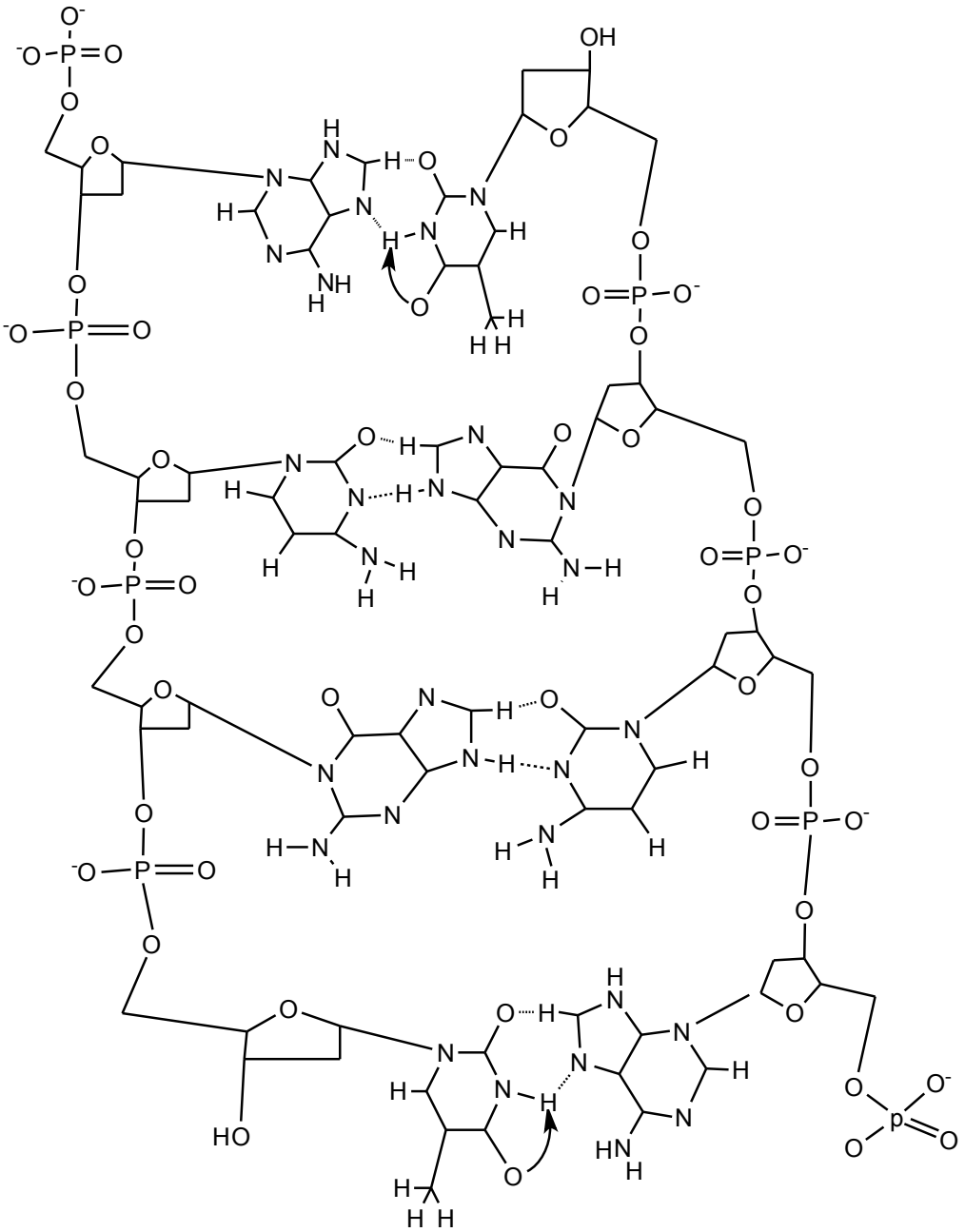


WATSON CRICK BASE PAIRING

Figure 5

Then the experiment is done to compare the energies for standard Watson-Crick base pairing (Figure 6) and that for Mark E. Curtis model (Figure 7). The optimizations of the structures were carried out in presence of water to imitate the natural environment of DNA inside the cells.


DNA



Curtis's proposed model of DNA base pairing.

Results

The pointers of the results inferred from the molecular dynamics simulations are presented below

1. GC base pairing proposed by Curtis can be stabilized by water-mediated hydrogen bonding.

(Water-mediated hydrogen bond plays important role in a molecular dynamics simulation. They are more labile; they break more easily and are rapidly replaced by another water molecule. One has to select a particular residue and all water molecules to find out how many hydrogen bonds are established, but will not find which specific water molecules and how many are involved).

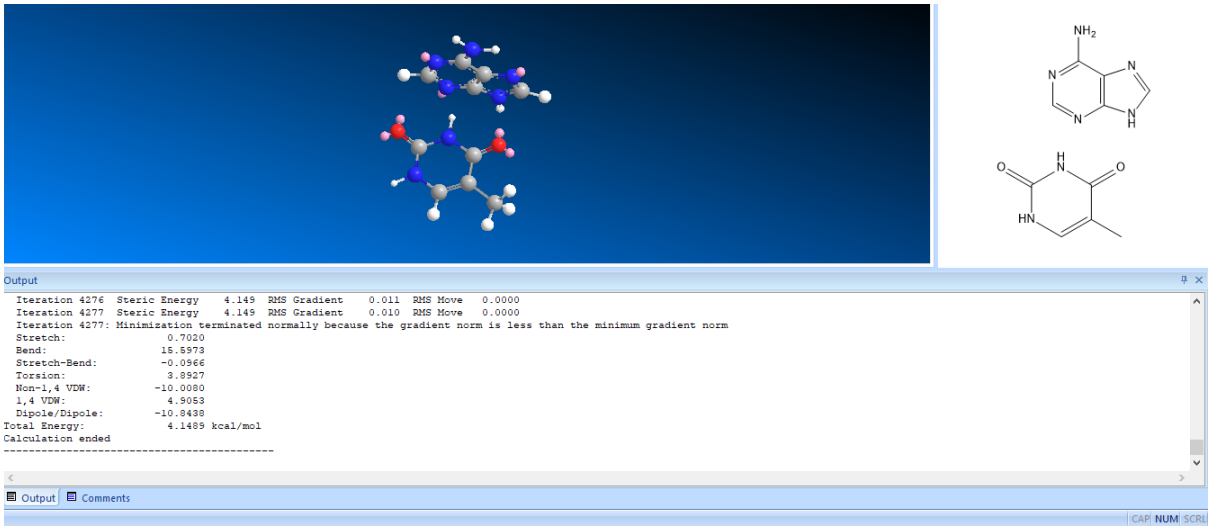
2. Results from the simulation study revealed that the –CH and =O interaction is not so significant.
3. The total energy of the entire test performed as per Curtis's suggestion for alternative base pairing are represented along with their simulation results.
4. Curtis model simulation is possible only in the presence of water. Total energy (E) was found to be 160.354Kcal/Mole and Vanderwall's interaction force was found to be -55.2739Kcal/Mole for GC base pairing. Similarly, for AT base pairing the total energy was found to be -54.9962Kcal/Mole and Vanderwall's interaction force was found to be -139.967Kcal/Mole.
5. The molecular dynamics simulation for Watson Crick DNA model in the presence of water revealed that the total energy was found to be 3089.57 Kcal/Mole and that for Mark E. Curtis model was found to be 3329.96 Kcal/Mole. Both the models are energetically close to each other. However, the symmetry of Curtis's model is better

than the Watson - Crick Model. Therefore, Curtis's hypothesis of the alternative structure of DNA cannot be discarded right away.

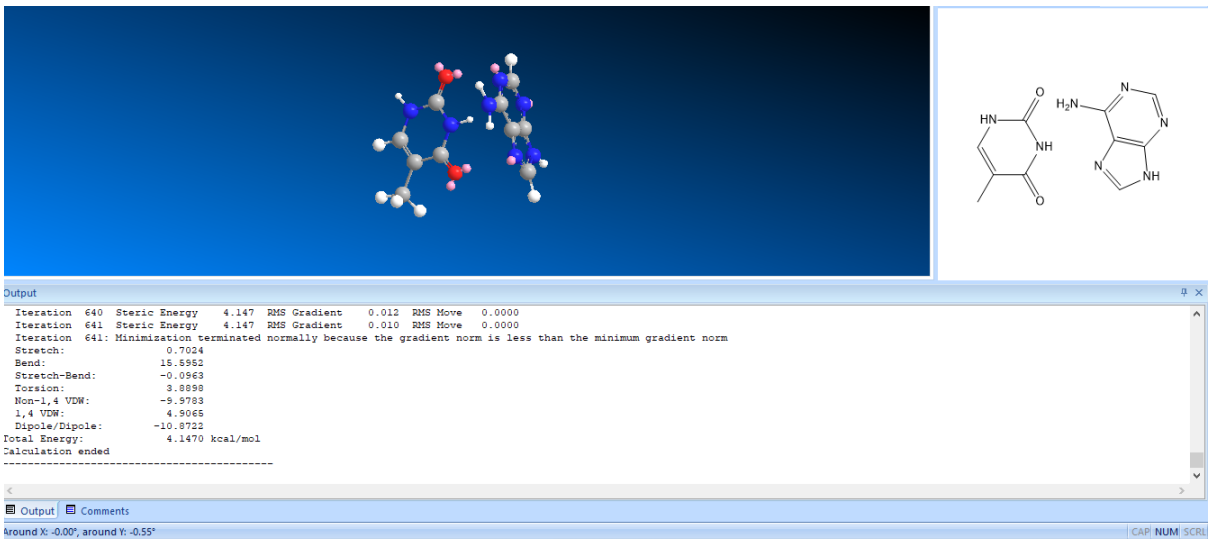
Table 1. The Vanderwall's interaction among the nucleotides in the aqueous environment and the corresponding energy (E) after a simulation in the **Ascalaph Designer software** using the **Amber94 force field algorithm**. The four nucleotide length DNA also simulated in the aqueous environment and their corresponding energy is listed in the table.

Simulation Characters	**Enthalpy (E) in Kcal/Mole for Watson-Crick (WC) Base Pairing**	**Enthalpy (E) in Kcal/Mole for Mark Curtis (MC) Base Pairing**	**The difference in Enthalpy (ΔE=WC-MC)**	**Inference**
Adenine (A) and Thiamine (T)	-88.216	-139.967	51.751	MC is more stable compared to WC
Guanine (G) and Cytosine (C)	-59.7357	-55.2739	-4.4618	WC is more stable compared to MC
Four Nucleotide length double helix in an aqueous environment	3089.57	3329.96	-240.39	WC is more stable compared to MC

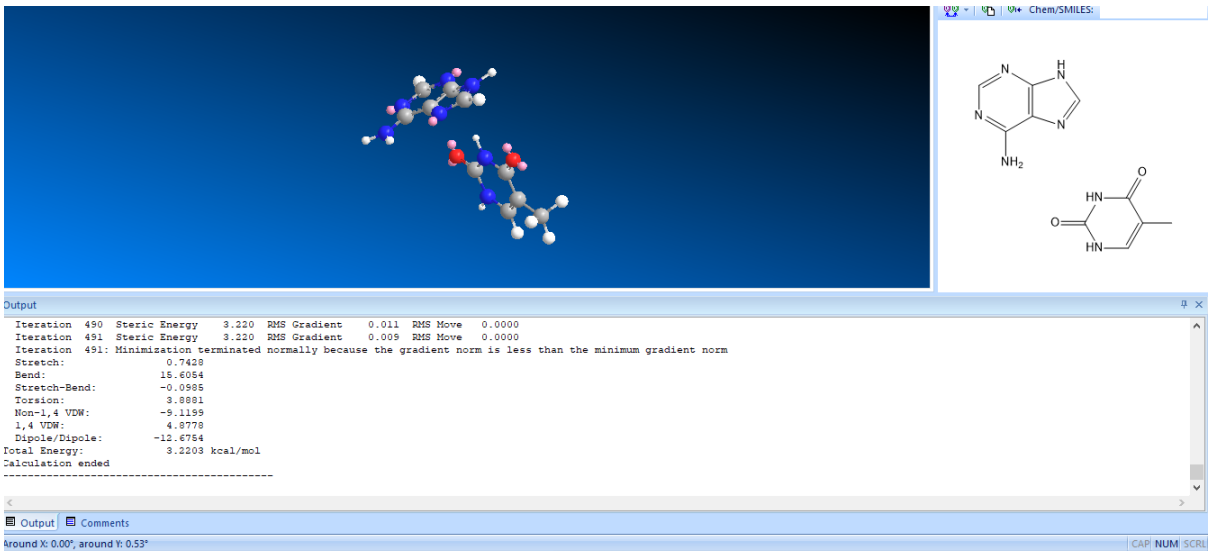
Molecular dynamics simulations of Adenine and Thiamine in Vacuum


Output
Iteration 4276 Steric Energy 4.149 RMS Gradient 0.011 RMS Move 0.0000
Iteration 4277 Steric Energy 4.149 RMS Gradient 0.010 RMS Move 0.0000
Iteration 4277: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.7020
Bend: 15.5973
Stretch-Bend: -0.0966
Torsion: 3.8927
Non-1,4 VDW: -10.0080
1,4 VDW: 4.9053
Dipole/Dipole: -10.8438
Total Energy: 4.1489 kcal/mol
Calculation ended
Output
Comments
CAP NUM SCRL

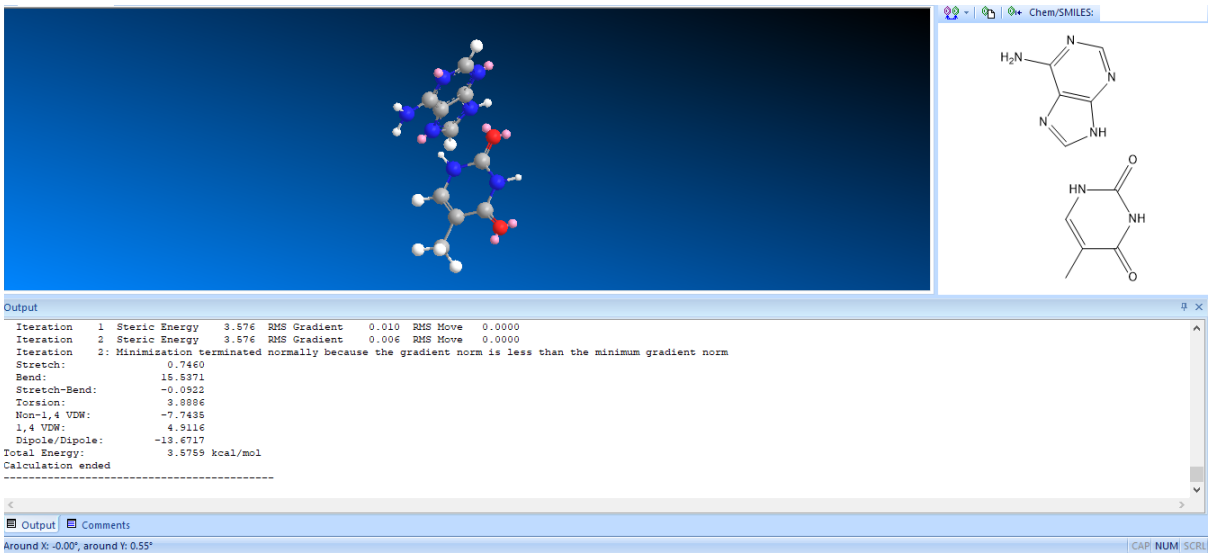
Total Energy: 4.1489 Kcal/Mole


Output
Iteration 640 Steric Energy 4.147 RMS Gradient 0.012 RMS Move 0.0000
Iteration 641 Steric Energy 4.147 RMS Gradient 0.010 RMS Move 0.0000
Iteration 641: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.7024
Bend: 15.5952
Stretch-Bend: -0.0963
Torsion: 3.8898
Non-1,4 VDW: -9.9783
1,4 VDW: 4.9065
Dipole/Dipole: -10.8722
Total Energy: 4.1470 kcal/mol
Calculation ended
Output
Comments
CAP NUM SCRL

Total Energy: 4.147 Kcal/Mole

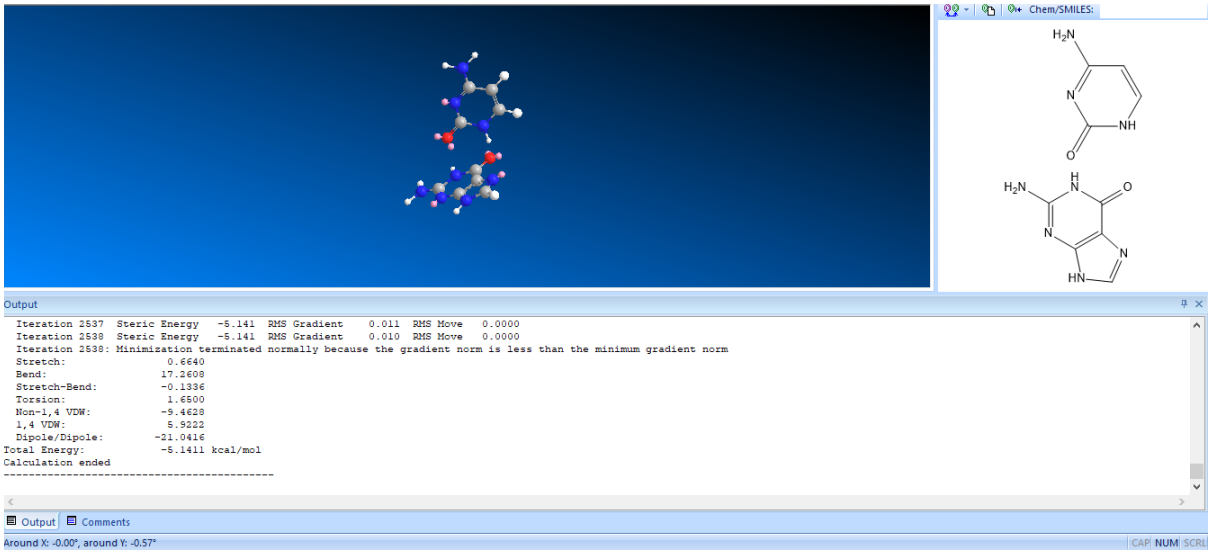

Chem/SMILES:
Output
Iteration 490 Steric Energy 3.220 RMS Gradient 0.011 RMS Move 0.0000
Iteration 491 Steric Energy 3.220 RMS Gradient 0.009 RMS Move 0.0000
Iteration 491: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.7428
Bend: 15.6054
Stretch-Bend: -0.0985
Torsion: 3.8801
Non-1,4 VDW: -9.1199
1,4 VDW: 4.8778
Dipole/Dipole: -12.6754
Total Energy: 3.2203 kcal/mol
Calculation ended
Output
Comments

Total Energy: 3.2203 Kcal/Mole

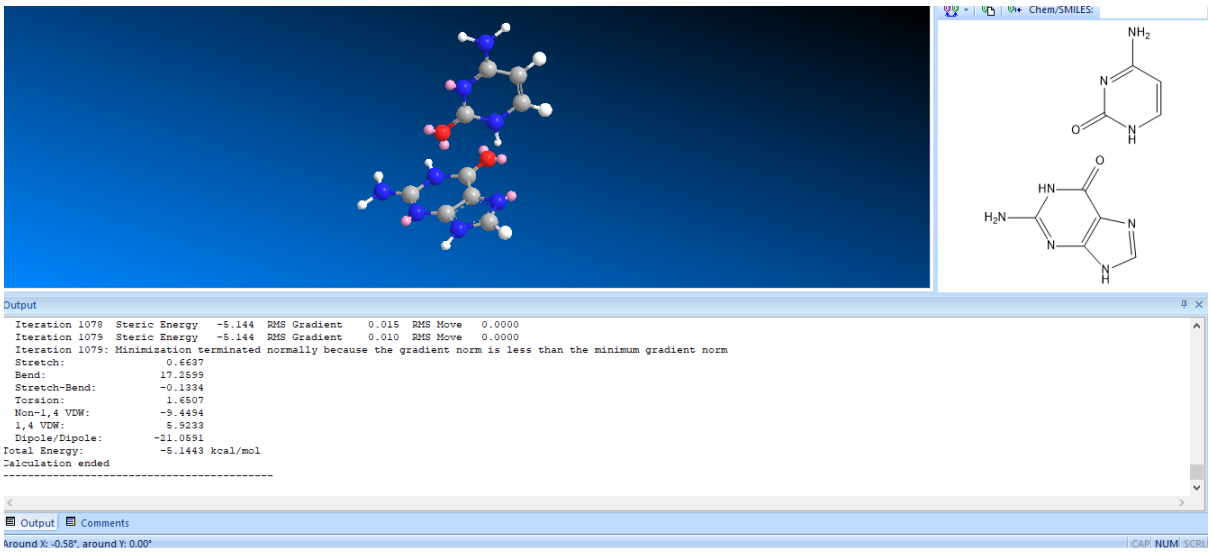

Chem/SMILES:
Output
Iteration 1 Steric Energy 3.576 RMS Gradient 0.010 RMS Move 0.0000
Iteration 2 Steric Energy 3.576 RMS Gradient 0.006 RMS Move 0.0000
Iteration 2: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.7460
Bend: 15.5371
Stretch-Bend: -0.0922
Torsion: 3.8886
Non-1,4 VDW: -7.7435
1,4 VDW: 4.9116
Dipole/Dipole: -13.6717
Total Energy: 3.5759 kcal/mol
Calculation ended
Output
Comments

Total Energy: 3.5759 Kcal/Mole

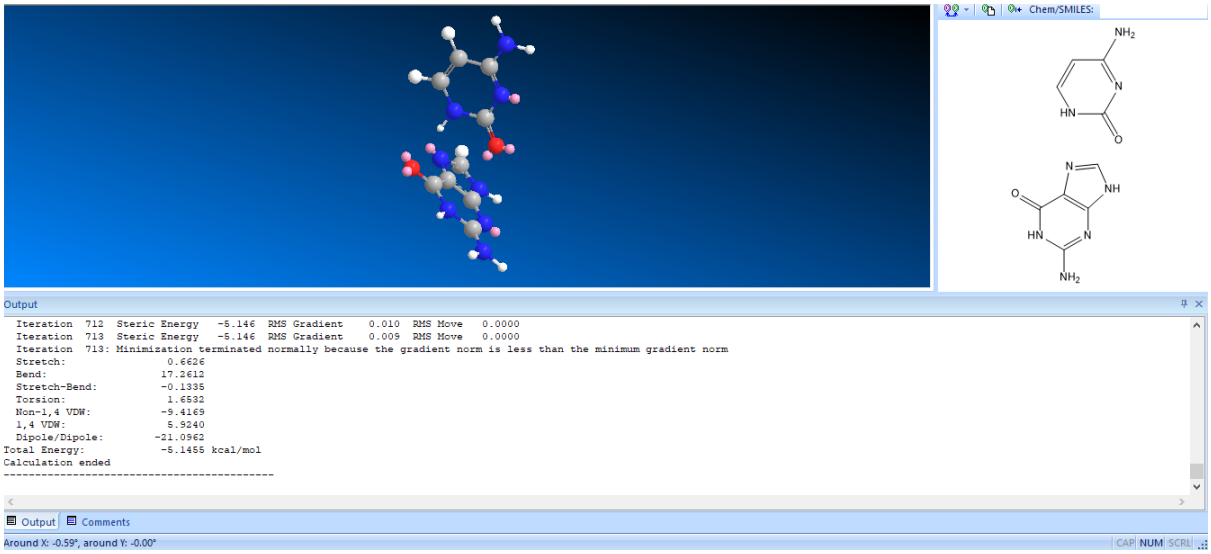
Molecular Dynamic simulations of Guanine and Cytosine in Vacuum


Chem/SMILES:
Output
Iteration 2537 Steric Energy -5.141 RMS Gradient 0.011 RMS Move 0.0000
Iteration 2538 Steric Energy -5.141 RMS Gradient 0.010 RMS Move 0.0000
Iteration 2538: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.6640
Bend: 17.2608
Stretch-Bend: -0.1336
Torsion: 1.6500
Non-1,4 VDW: -9.4628
1,4 VDW: 5.9222
Dipole/Dipole: -21.0416
Total Energy: -5.1411 kcal/mol
Calculation ended
Output
Comments

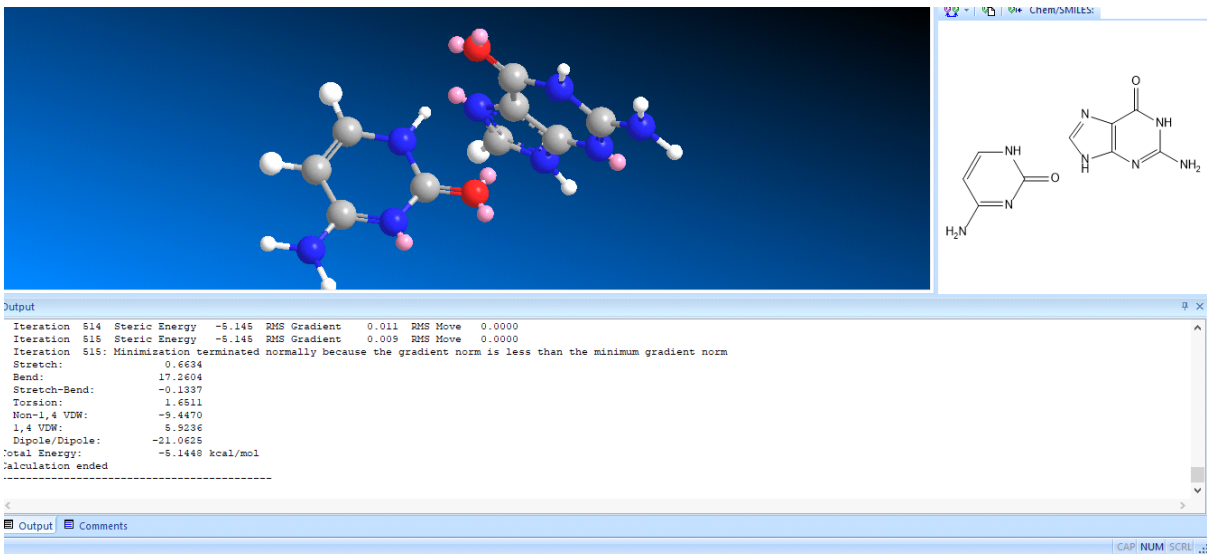
Total energy -5.1411Kcal/Mole


Chem/SMILES:
Output
Iteration 1078 Steric Energy -5.144 RMS Gradient 0.015 RMS Move 0.0000
Iteration 1079 Steric Energy -5.144 RMS Gradient 0.010 RMS Move 0.0000
Iteration 1079: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.6637
Bend: 17.2599
Stretch-Bend: -0.1334
Torsion: 1.6507
Non-1,4 VDW: -9.4494
1,4 VDW: 5.9233
Dipole/Dipole: -21.0591
Total Energy: -5.1443 kcal/mol
Calculation ended
Output
Comments

Total energy -5.1443Kcal/Mole

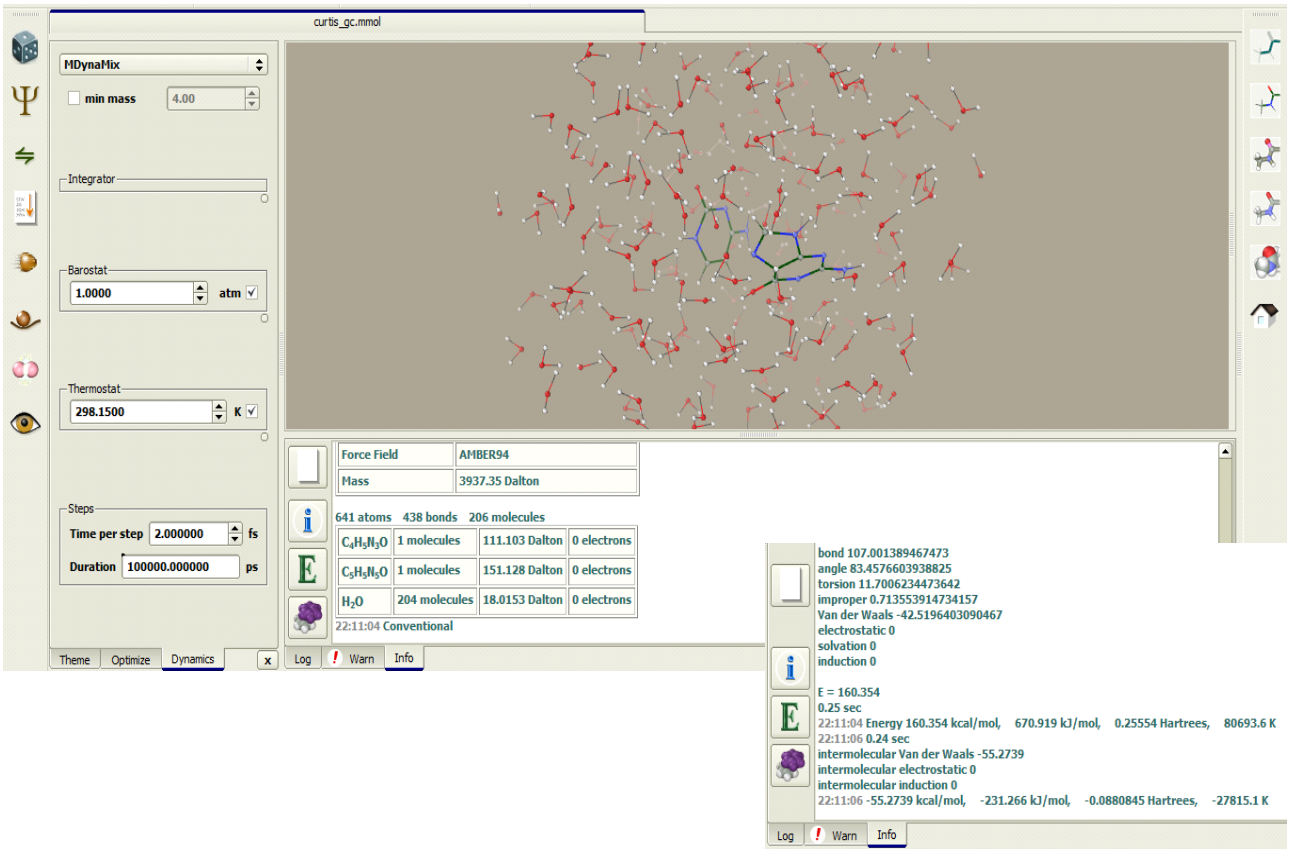

Chem/SMILES:
Output
Iteration 712 Steric Energy -5.146 RMS Gradient 0.010 RMS Move 0.0000
Iteration 713 Steric Energy -5.146 RMS Gradient 0.009 RMS Move 0.0000
Iteration 713: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.6626
Bend: 17.2612
Stretch-Bend: -0.1335
Torsion: 1.6532
Non-1,4 VDW: -9.4169
1,4 VDW: 5.9240
Dipole/Dipole: -21.0962
Total Energy: -5.1455 kcal/mol
Calculation ended
Output
Comments

Total energy: -5.1455Kcal/Mole

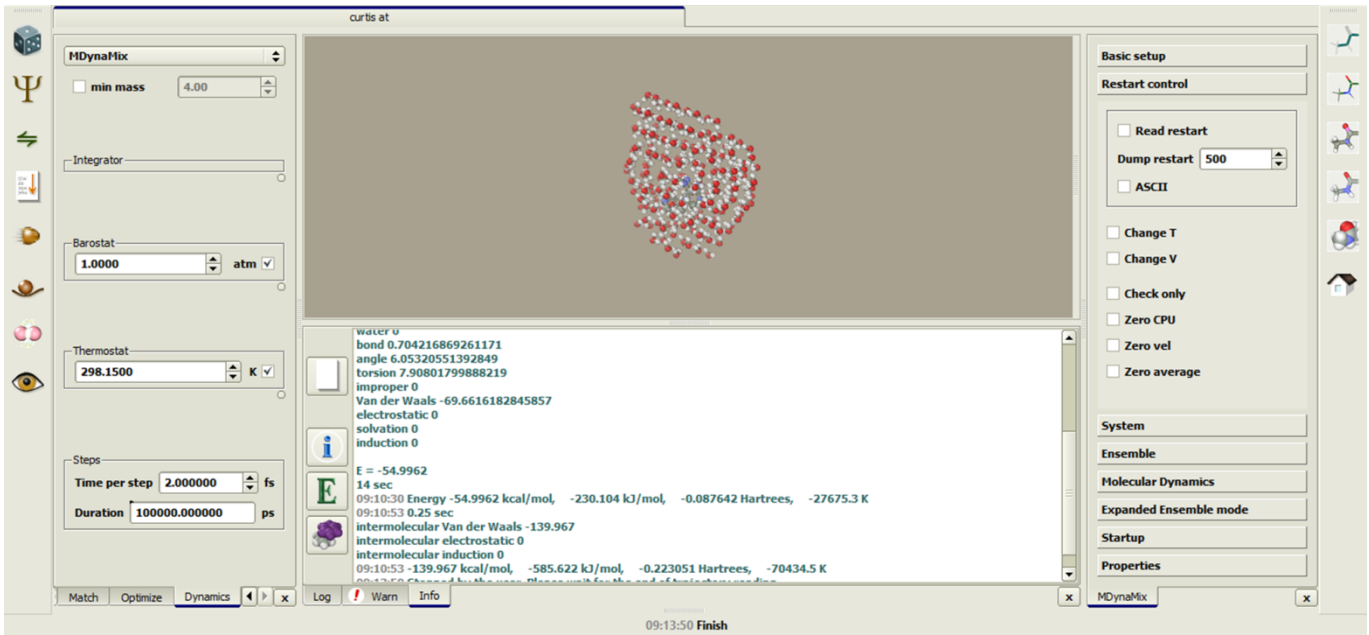

Output
Iteration 514 Steric Energy -5.145 RMS Gradient 0.011 RMS Move 0.0000
Iteration 515 Steric Energy -5.145 RMS Gradient 0.009 RMS Move 0.0000
Iteration 515: Minimization terminated normally because the gradient norm is less than the minimum gradient norm
Stretch: 0.6634
Bend: 17.2604
Stretch-Bend: -0.1337
Torsion: 1.6511
Non-1,4 VDW: -9.4470
1,4 VDW: 5.9236
Dipole/Dipole: -21.0625
Total Energy: -5.1448 kcal/mol
Calculation ended
Output
Comments

Total energy: -5.1448Kcal/Mole

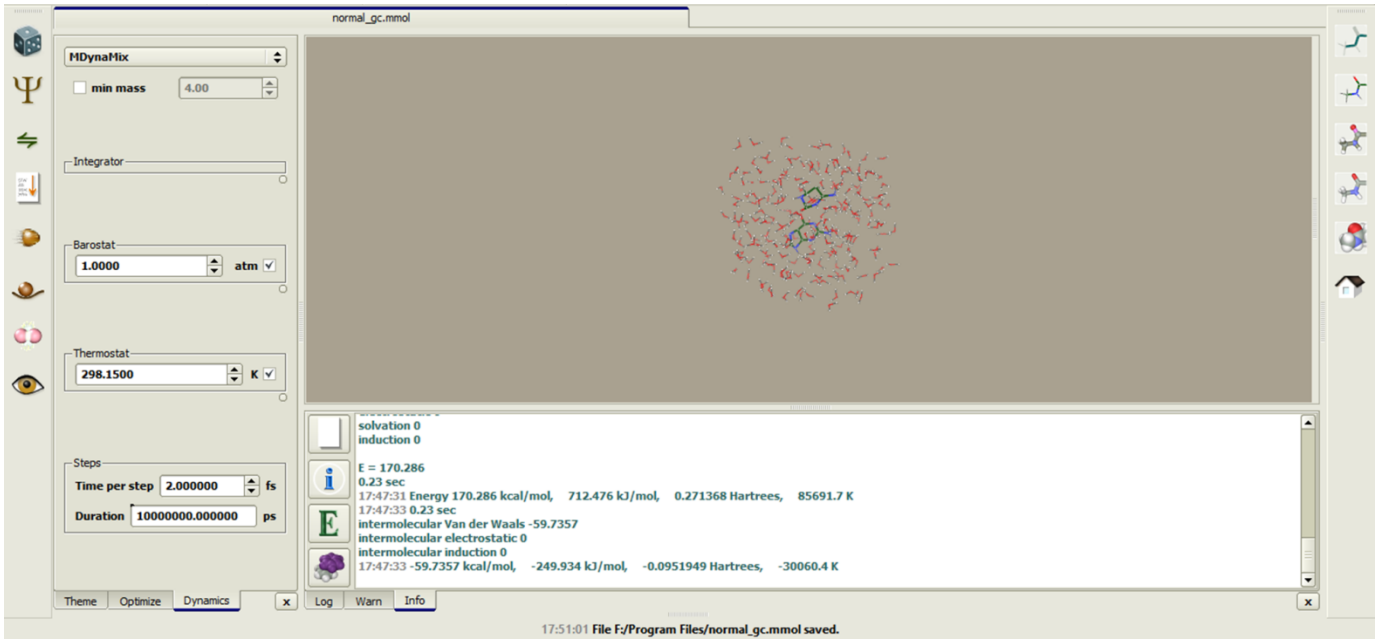
Molecular Dynamics simulations of the nucleotide pairs in the aqueous environment



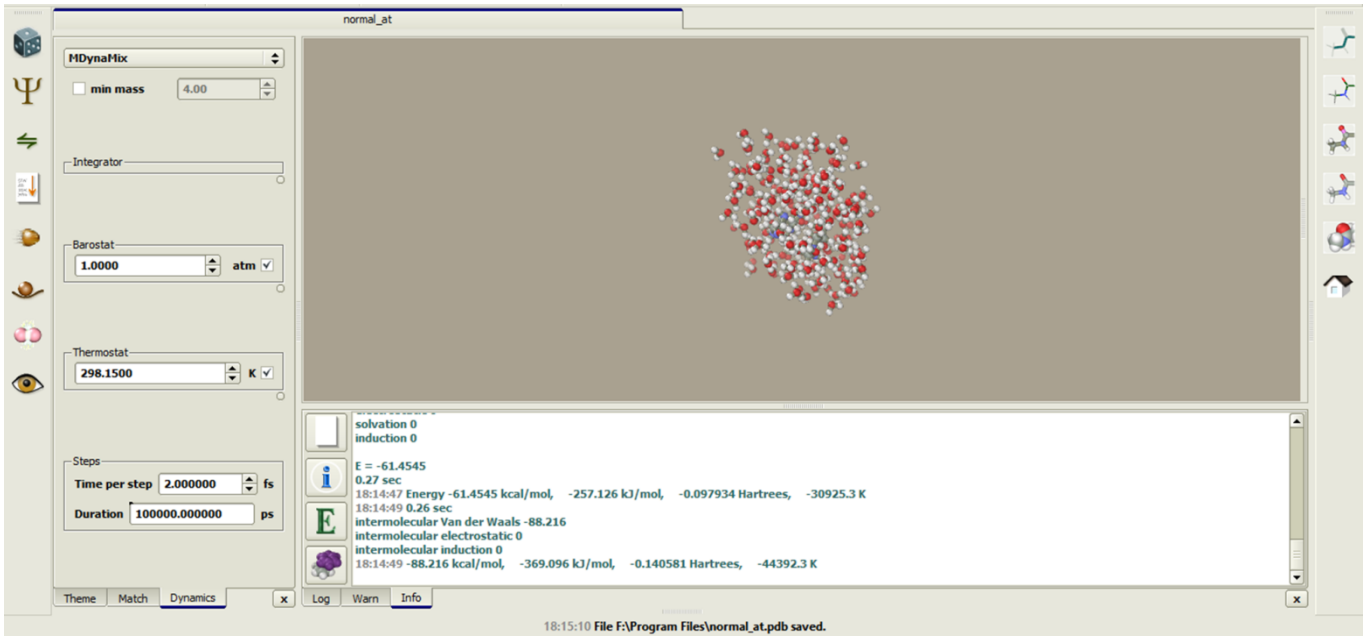
Curtis's GC Base pairing simulation in the aqueous environment.



Curtis's AT Base pairing simulation in the aqueous environment.

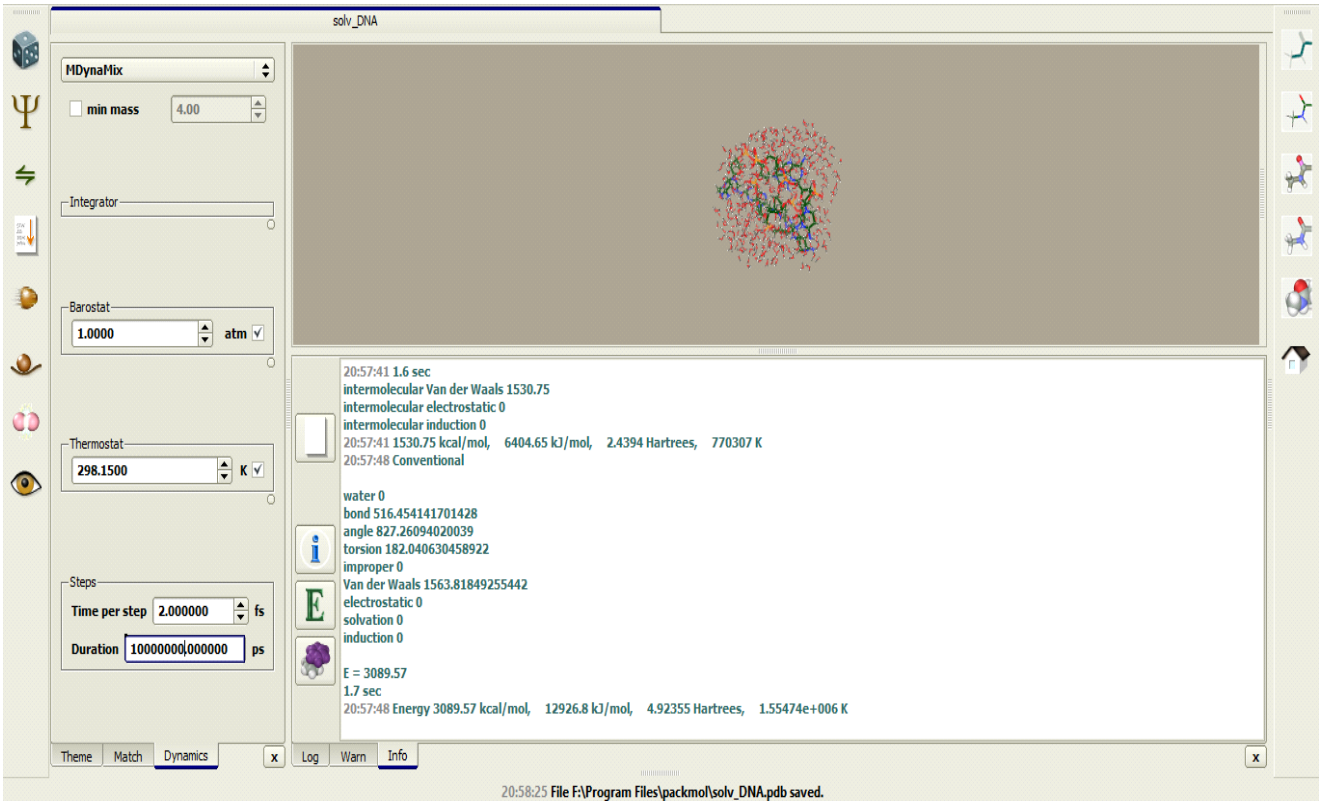


Watson-Crick's GC Base pairing simulation in the aqueous environment.

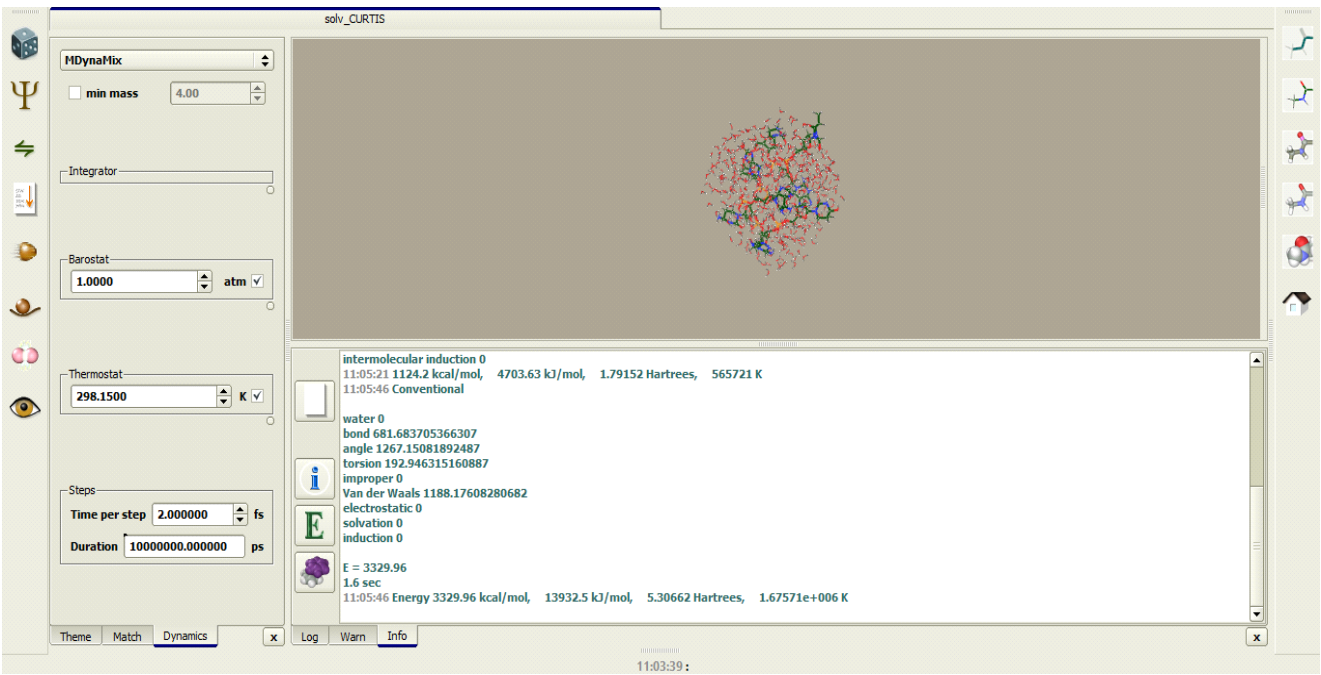


Watson-Crick's AT base pairing simulation in the aqueous environment.

Molecular Dynamic simulation of the four nucleotide DNA of the Watson-Crick and Curtis's base pairing



Molecular Dynamic simulation of the four nucleotide DNA of the Watson-Crick base pairing



Molecular Dynamic simulation of the four nucleotide DNA of Curtis's base pairing

Conclusion:

From the theoretical calculation, it was found that the total energy of both the DNA models is comparable in the aqueous environment. However, the AT base pairing as per the Curtis's model is found to be more stable compared to the Watson-Crick base pairing. The GC base pairing in the Watson-Crick's model is slightly more stable compared to Curtis's model. Therefore, Curtis's hypothesis on the alternative structure of the DNA cannot be discarded.

References

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